CLAIMS

What is claimed is:

1. A peptide fragment of a viral Macrophage Inflammatory Protein-II (vMIP-II) (SEQ. ID. NO: 1), wherein said fragment selectively prevents CXCR4 signal transduction and coreceptor function in mediating an entry of an HIV-1.

2. The peptide fragment of **Claim 1**, wherein said fragment comprises an amino-terminal end of said vMIP-II.

3. The peptide fragment of **Claim 2**, wherein said amino-terminal end comprises amino acid residues 1-21 (V1, SEQ ID NO: 2), or any subfragments therein.

4. The peptide fragment of **Claim 1**, wherein said fragment is a lead compound for development of novel small molecular agents to prevent HIV-1 from entering a cell.

5. A peptide of the formula

$X\text{-}R_1\text{-}R_2\text{-}R_3\text{-}R_4\text{-}R_5\text{-}R_6\text{-}R_7\text{-}R_8\text{-}R_9\text{-}R_{10}\text{-}R_{11}\text{-}R_{12}\text{-}R_{13}\text{-}R_{14}\text{-}R_{15}\text{-}R_{16}\text{-}R_{17}\text{-}R_{18}\text{-}R_{19}\text{-}R_{20}\text{-}R_{21}\text{-}Y$

wherein:

X is a substituent attached on the N-terminal of a peptide, X can be H, CH_3CO, C_6H_5CO, or $C_6H_5CH_2CO$;

Y is a substituent attached on the C-terminal of a peptide with the following general structure,

$C(\alpha)\text{-}CO\text{-}Y$

Y can be OH, NH_2, OCH_3, $OCH_2C_6H_5$, or $NHCH_3$; Y can be from zero to nine amino acids,

R_1 is Ile, Leu, Val, or Phe;

R_2 is Gly, Ala;
R_3 is Ala, Gly;
R_4 is Ser, Thr, or Tyr;
R_5 is Trp, Phe, Tyr;
R_6 is His, Lys, Arg, or Tyr;
R_7 is Arg, His, or Lys;
R_8 is Pro, Leu, or Val;
R_9 is Asp, Glu, Arg, or Lys;
R_{10} is Lys, Arg, or His;
R_{11} is Cys, Ser, or Ala;
R_{12} is Cys, Ser, or Ala;
R_{13} is Ile, Leu, or Val;
R_{14} is Gly, Ala;
R_{15} is Tyr, Thr, Ser;
R_{16} is Gln, Asn, Arg, or Lys;
R_{17} is Lys, Arg, or His;
R_{18} is Arg, His, or Lys;
R_{19} is Pro, Leu, or Val;
R_{20} is Ile, Leu, or Val;
R_{21} is Pro, Leu, or Val;
and if R_{11} is Cys then R_{12} can be Cys, penicillamine or tertiary butyloxycarbonyl-a-aminobutyric acid;
if R_{12} is Cys then R_{11} can be Cys, penicillamine, tertiary butyloxycarbonyl-a-aminobutyric acid, and,
R_{11} and R_{12} can be penicillamine, or tertiary butyloxycarbonyl-a-aminobutyric acid;
and, R_{11} and R_{12} can be Ala.

6. The peptide of **Claim** 5, wherein a preferred embodiment, comprises
X can be H, or CH_3CO; Y can be OH,or NH_2; and,R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_6 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is

Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

7. The peptide of **Claim 5**, wherein a most preferred embodiment, comprises X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

8. The peptide of **Claim 5**, wherein a preferred embodiment comprises a C-terminal truncation peptide contaiings at least the following fragment:

X-R_1-R_2-R_3-R_4-R_5-R_6-R_7-R_8-Y, and wherein;

R_1 is Ile, Leu, or Phe;

R_2 is Gly, Ala, or Val;

R_3 is Ala, Val, or Gly;

R_4 is Ser, Thr, or Tyr;

R_5 is Trp, Phe, Tyr, or Leu;

R_6 is His, Lys, Arg, or Trp;

R_7 is Arg, His, or Lys;

R_8 is Pro, Leu, or Val.

and, a C-terminal truncation peptide preferably containing at least a following fragment, wherein X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys.

9. The peptide of **Claim 1**, wherein said peptide comprises between 3-30 amino acids, preferably 8-21 amino acids.

10. A synthetic peptide, wherein each amino acid of said synthetic peptide is a D amino acid, having the formula:

X-R_{1d}-R_{2d}-R_{3d}-R_{4d}-R_{5d}-R_{6d}-R_{7d}-R_{8d}-R_{9d}-R_{10d}-R_{11d}-R_{12d}-R_{13d}-R_{14d}-R_{15d}-R_{16d}-R_{17d}-R_{18d}-R_{19d}-R_{20d}-R_{21d}-Y, wherein,

X is a substituent attached on the N-terminal of a peptide, X can be H, CH_3CO, C_6H_5CO, or $C_6H_5CH_2CO$; and

Y is a substituent attached on the C-terminal of a peptide with the following general structure:

$C(\alpha)$-CO-Y, wherein Y can be OH, NH_2, OCH_3, $OCH_2C_6H_5$, or $NHCH_3$ and Y can be from zero to nine amino acids.

R_{1d} is Ile, Leu, Val, or Phe;

R_{2d} is Gly, Ala;

R_{3d} is Ala, Gly;

R_{4d} is Ser, Thr, or Tyr;

R_{5d} is Trp, Phe, or Tyr;

R_{6d} is His, Lys, Arg, or Tyr;

R_{7d} is Arg, His, or Lys;

R_{8d} is Pro, Leu, or Val;

R_{9d} is Asp, Glu, Arg, or Lys;

R_{10d} is Lys, Arg, or His;

R_{11d} is Ala, Cys, or Ser;

R_{12d} is Ala, Cys, or Ser;

R_{13d} is Ile, Leu, or Phe;

R_{14d} is Gly, Ala;

R_{15d} is Tyr, Thr, Ser;

R_{16d} is Gln, Asn, Arg, or Lys;

R_{17d} is Lys, Arg, or His;

R_{18d} is Arg, His, or Lys;

R_{19d} is Pro, Leu, or Val;

R_{20d} is Ile, Leu, or Val;

R_{21d} is Pro, Leu, or Val;

and wherein:

if R_{11d} is Cys then R_{12d} can be Cys, penicillamine or tertiary butyloxycarbonyl-a-aminobutyric acid;

if R_{12d} is Cys then R_{11d} can be Cys, penicillamine, or tertiary butyloxycarbonyl-a-aminobutyric acid;

and,

R_{11d} and R_{12d} can be penicillamine, or tertiary butyloxycarbonyl-a-aminobutyric acid;

and, R_{11d} and R_{12d} can be Ala.

11. The peptide of **Claim 10**, wherein a preferred embodiment comprises the following formula:

X can be H, CH_3CO; Y can be OH, or NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

12. The peptide of **Claim 10**, wherein a most preferred embodiment comprises the following formula:

X is H, Y is NH_2; and,R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

13. The peptide of **Claim 10**, wherein a preferred C-terminal truncation peptide comprising at least the following fragment:

X-R_{1d}-R_{2d}-R_{3d}-R_{4d}-R_{5d}-R_{6d}-R_{7d}-R_{8d}-Y

and wherein;

R_{1d} is Ile, Leu, or Phe;

R_{2d} is Gly, Ala, or Val;

R_{3d} is Ala, Val, or Gly;

R_{4d} is Ser, Thr, or Tyr;

R_{5d} is Trp, Phe, Tyr, or Leu;

R_{6d} is His, Lys, Arg, or Trp;

R_{7d} is Arg, His, or Lys;

R_{8d} is Pro, Leu, or Val.

14. The peptide of **Claim 10**, wherein a more preferably C-terminal truncation peptide comprises at least the following fragment; X is H, Y is NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys.

15. The peptide of **Claim 10**, comprising between 3-30 amino acids, preferably 8-21 amino acids.

16. The peptide of **Claim 5**, wherein said peptide comprises a reversed form of said formula, comprising,
$X\text{-}R_{21}\text{-}R_{20}\text{-}R_{19}\text{-}R_{18}\text{-}R_{17}\text{-}R_{16}\text{-}R_{15}\text{-}R_{14}\text{-}R_{13}\text{-}R_{12}\text{-}R_{11}\text{-}R_{10}\text{-}R_9\text{-}R_8\text{-}R_7\text{-}R_6\text{-}R_5\text{-}R_4\text{-}R_3\text{-}R_2\text{-}R_1\text{-}Y$
wherein an amino acid is in an L form or as naturally occurring amino acid.

17. The peptide of **Claim 16**, wherein a preferred embodiment, comprises
X can be H, or CH_3CO; Y can be OH,or NH_2; and,R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

18. The peptide of **Claim 16**, wherein a most preferred embodiment, comprises X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys, R_{11} is Cys, R_{12} is Cys, R_{13} is Leu, R_{14} is Gly, R_{15} is Tyr, R_{16} is Gln, R_{17} is Lys, R_{18} is Arg, R_{19} is Pro, R_{20} is Leu, R_{21} is Pro.

19. The peptide of **Claim 16**, wherein a preferred embodiment comprises a C-terminal truncation peptide contaiings at least the following fragment:

X-R_1-R_2-R_3-R_4-R_5-R_6-R_7-R_8-Y, and wherein;

R_1 is Ile, Leu, or Phe;

R_2 is Gly, Ala, or Val;

R_3 is Ala, Val, or Gly;

R_4 is Ser, Thr, or Tyr;

R_5 is Trp, Phe, Tyr, or Leu;

R_6 is His, Lys, Arg, or Trp;

R_7 is Arg, His, or Lys;

R_8 is Pro, Leu, or Val.

and, a C-terminal truncation peptide preferably containing at least a following fragment, wherein X is H, Y is NH_2; and, R_1 is Leu, R_2 is Gly, R_3 is Ala, R_4 is Ser, R_5 is Trp, R_6 is His, R_7 is Arg, R_8 is Pro, R_9 is Asp, R_{10} is Lys.

20. The peptide of **Claim 16**, wherein said peptide comprises between 3-30 amino acids, preferably 8-21 amino acids.

21. The peptide of **Claim 5**, wherein said peptide comprises a reversed form of said formula, comprising X-R_{21d}-R_{20d}-R_{19d}-R_{18d}-R_{17d}-R_{16d}-R_{15d}-R_{14d}-R_{13d}-R_{12d}-R_{11d}-R_{10d}-R_{9d}-R_{8d}-R_{7d}-R_{6d}-R_{5d}-R_{4d}-R_{3d}-R_{2d}-R_{2d}-Y, wherein an amino acid is in a D form or as an unnaturally occurring amino acid.

22. The peptide of **Claim 21**, wherein a preferred embodiment comprises the following formula:

X can be H, CH_3CO; Y can be OH, or NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

23. The peptide of **Claim 21**, wherein a most preferred embodiment comprises the following formula:
X is H, Y is NH_2; and,R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys, R_{11d} is Ala, R_{12d} is Cys, R_{13d} is Leu, R_{14d} is Gly, R_{15d} is Tyr, R_{16d} is Gln, R_{17d} is Lys, R_{18d} is Arg, R_{19d} is Pro, R_{20d} is Leu, R_{21d} is Pro.

23. The peptide of **Claim 21**, wherein a preferred C-terminal truncation peptide comprising at least the following fragment:
X-R_{1d}-R_{2d}-R_{3d}-R_{4d}-R_{5d}-R_{6d}-R_{7d}-R_{8d}-Y
and wherein;
R_{1d} is Ile, Leu, or Phe;
R_{2d} is Gly, Ala, or Val;
R_{3d} is Ala, Val, or Gly;
R_{4d} is Ser, Thr, or Tyr;
R_{5d} is Trp, Phe, Tyr, or Leu;
R_{6d} is His, Lys, Arg, or Trp;
R_{7d} is Arg, His, or Lys;
R_{8d} is Pro, Leu, or Val.

24. The peptide of **Claim 21**, wherein a more preferably C-terminal truncation peptide comprises at least the following fragment;
X is H, Y is NH_2; and, R_{1d} is Leu, R_{2d} is Gly, R_{3d} is Ala, R_{4d} is Ser, R_{5d} is Trp, R_{6d} is His, R_{7d} is Arg, R_{8d} is Pro, R_{9d} is Asp, R_{10d} is Lys.

25. The peptide of **Claim 21**, comprising between 3-30 amino acids, preferably 8-21 amino acids.

26. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 5**.

27. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 10**.

28. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 16**.

29. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a peptide according to **Claim 21**.

30. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 5**.

31. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 10**.

32. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 16**.

33. A method of inhibiting entry of HIV-1 into CXCR4-expressing cells, comprising contacting said cells with a peptide according to **Claim 21**.

34. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 5.**

35. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 10**.

36. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 16**.

36. A method of treating infection by HIV-1, comprising administering to an individual an effective amount of a peptide according to **Claim 21**.

37. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising contacting said cells with a peptide according to **Claim 5**

38. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising contacting said cells with a peptide according to **Claim 10**.

39. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising contacting said cells with a peptide according to **Claim 16**.

40. A method of inhibiting a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising contacting said cells with a peptide according to **Claim 21**.

41. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 5**.

42. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 10**.

43. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 46**.

44. A method of treating a disease, a causative agent of said disease requiring entry into CXCR4-expressing cells via CXCR4, comprising administering to an individual an effective amount of a peptide according to **Claim 21**.